CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-128

CHEMISTRY REVIEW(S)

DIVISION OF ANTI-INFLAMMATORY, ANALGESI AND OPTHALMIC DRUG PRODUCTS (HFD-550)

Review of Chemistry, Manufacturing, and Controls

NDA #: 21-128 **DATE REVIEWED:** 7/19/00
REVIEW #: 1 **REVIEWER:** Rao Puttagunta

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE
ORIGINAL	30-SEP-1999	01-OCT-1999	15-OCT-1999
AMENDMENTS	16-NOV-1999	17-NOV-1999	
	11-FEB-2000	14-FEB-2000	
	27-APR-2000	28-APR-2000	
	07-JUL-2000	10-JUL-2000	
	11-JUL-2000		
	17-JUL-2000		

NAME & ADDRESS OF APPLICANT:

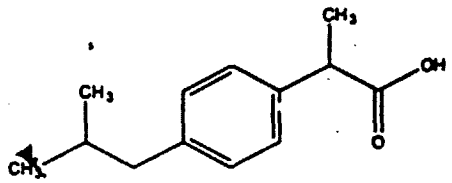
McNeil Consumer Healthcare
7050 Camp Hill Road
Fort Washington, PA 19034

DRUG PRODUCT NAME:

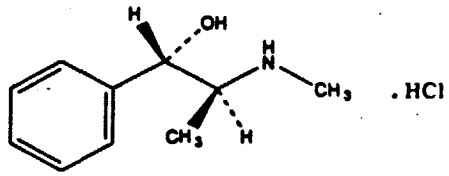
Proprietary: Children's Motrin Cold Suspension
Established: Ibuprofen/Pseudoephedrine HCl
Code Name/#: N/A
Chem.Type/Ther.Class: 3 S

PHARMACOL. CATEGORY/INDICATION: Common cold, Flu or Sinusitis, and Fever
DOSAGE FORM: Suspension
STRENGTHS: Ibuprofen 100mg/5mL, Pseudoephedrine HCl 15mg/5mL
ROUTE OF ADMINISTRATION: Oral
Rx/OTC: __Rx _X_OTC
SPECIAL PRODUCTS: __Yes _X_No

CHEMICAL NAME; STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:



Ibuprofen:
(±)-2-(p-Isobutylphenyl)propionic acid,
$C_{13}H_{18}O_2$, mol.wt. 206.28



Pseudoephedrine HCl:
Benzenemethanol, α-[1-(methylamino)ethyl] - [S-(R*, R*)]-,, hydrochloride, $C_{10}H_{15}NO.HCl$, mol.wt. 201.69

SUPPORTING DOCUMENTS:

DMF Type/ Number	Item/Component	Holder	Status	Review Date	LOA Date
	Pseudoephedrine HCl		Adequate	1/04/00	10/29/98
	Ibuprofen		Adequate	2/24/99	4/05/99
			Adequate (NDA 20516/S-003)	5/29/98	3/19/99
	Acesulfame potassium (No-calorie sweetener)		Adequate	4/15/00	2/08/99
			Adequate	7/14/00	3/16/99
			Adequate (NDA 20516/S-003)	5/29/98	3/05/99
			Adequate	7/14/00	3/16/99
			Complies with 21 CFR §177	N/A	1/27/99
			Complies with 21 CFR §177	N/A	2/05/99
			Complies with 21 CFR §117	N/A	8/25/99
			Complies with 21 CFR §177	N/A	2/03/99
			Complies with 21 CFR §177	N/A	2/23/99
	Container Manufacture		Complies with 21 CFR §177	N/A	1/29/99
			Complies with 21 CFR §177	N/A	1/29/99

RELATED DOCUMENTS: [redacted] NDA 19-899

CONSULTS/REQUESTS:

Request Type	Date Requested	Status
EER	03-DEC-99	OC Recommendation – Acceptable (See attached EER Summary Report)
Method Validation	7/12/00	Pending
OPDRA	N/A	N/A

Amendments

Date	Description
16-NOV-1999	Updated establishments' list and inspection readiness statement.
11-FEB-2000	1). List of samples to be submitted to the FDA 2). Preservative effectiveness data
27-APR-2000	Updated analytical methods
27-JUN-2000	Updated method validation package
07-JUL-2000	Withdrawal of package interchangeability protocol
11-JUL-2000	12-month stability data.
17-JUL-2000	18-month stability data and statistical analysis

REMARKS:

Drug substance: The NDA contains test methods and specifications. The sponsor refers to [redacted] for Ibuprofen USP, and [redacted] for Pseudoephedrine HCl USP. DMF authorization letters for the both drug substances are included.

The [redacted] for the drug substances were reviewed and found adequate.

Drug Product: The complete CMC information is provided. The stability data include 6-month accelerated, 18-month long term, and a 3-month –20 to +40°C cycle results.
Proposed expiration period is 36 months.

The DMFs [redacted] were reviewed and found adequate. The remaining inactive ingredients are same as those used for an approved formulation Children's MOTRIN (Ibuprofen) Suspension (NDA 20-516). The [redacted] used in the container, and the [redacted] used in the closer comply with 21 CFR § 177.1520 for Indirect Food Additives: Polymers. The proposed dissolution method and specifications [redacted] comply with USP 24 <711>, and are acceptable to the Biopharm reviewer Dr. Abi Adebowale [redacted]

CONCLUSIONS & RECOMMENDATIONS:

The information provided on the chemistry, manufacture and controls of the drug substance and drug product is adequate. The DMFs for the active ingredients were reviewed and found adequate. The methods validation is pending.

Recommendations:

1. The expiration period of 24 months is recommended at this time, and the future extension of the expiration period should be based on real time data.
2. From the chemistry stand point, the NDA is recommended for approval.

/S/

Rao Puttagunta, Ph.D., Review Chemist

/S/

Mona Zarifa, Ph.D., ActingTeam Leader